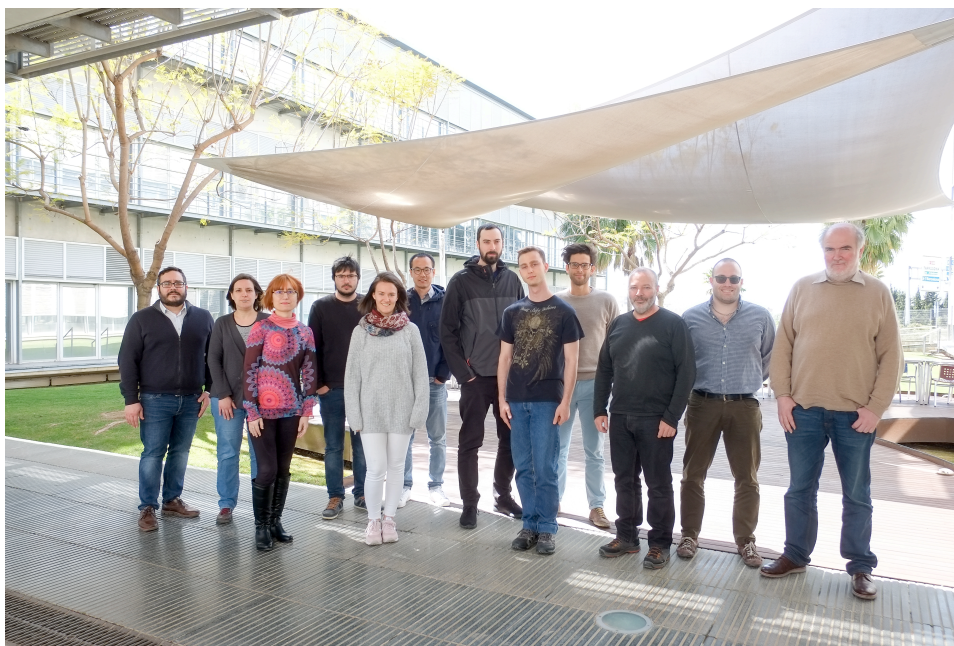


Maseras Research Group



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Abstract

Computational chemistry is applied to the study of different chemical processes of practical interest. DFT and DFT/MM methods are used to characterize different processes in

homogeneous catalysis, in most cases in collaboration with experimental groups. Studies in 2017 focused on single electron transfer processes, photoactivated reactions, and carbon-carbon bond formation.

Single electron transfer processes

The many oxidation-reduction steps homogeneous catalysis have been traditionally considered to operate through two-electron transfer steps. This view has been challenged in recent years, and we have been able to demonstrate in a number of cases the existence of more efficient reaction mechanisms based in single electron transfer.

The role of single electron transfer was highlighted in a collaboration with the group of Llobet (ICIQ) in water oxidation. The systematic computational study of the mechanism for water oxidation in four different complexes confirms the existence of an alternative mechanism for the O-O bond formation step to those previously reported: the single electron transfer - water nucleophilic attack (SET-WNA) (Fig. 1). The calculated mechanism relies on two SET steps, and features the existence of an intermediate with a $(\text{HO}\cdots\text{OH})^-$ moiety in the vicinity of the metal center. It is operative in at least three representative copper based complexes, and is the only option that explains the experimentally observed efficiency in two of them. The proposal of this reaction pathway redefines the mechanistic scenario and importantly, generates a promising avenue for designing more efficient water oxidation catalysts based on first row transition metals.

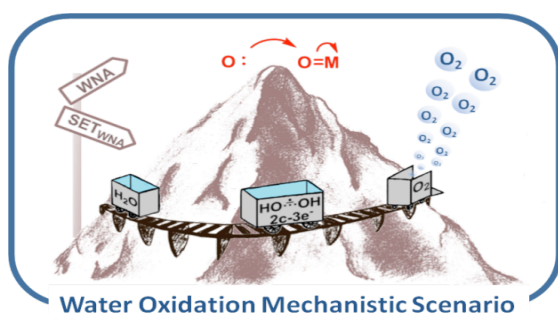


Fig. 1 – Single electron transfer is able to bypass the high barrier for water oxidation in a number of cases.

Single electron transfer processes also play a key role in the reaction of nickel complexes with halobenzene, which were investigated in collaboration with Nelson (Strathclyde, Glasgow). Density functional theory (DFT) calculations were used to study the oxidative addition of aryl halides to complexes of the type $[\text{Ni}(\text{PMe}_n\text{Ph}_{(3-n)})_4]$, revealing the crucial role of an

open shell singlet transition state for halide abstraction. The formation of Ni^{I} versus Ni^{II} was rationalised through the study of three different pathways: (i) halide abstraction by $[\text{Ni}(\text{PMe}_n\text{Ph}_{(3-n)})_3]$, via an open shell singlet transition state; (ii) $\text{S}_{\text{N}}2$ -type oxidative addition to $[\text{Ni}(\text{PMe}_n\text{Ph}_{(3-n)})_3]$, followed by phosphine dissociation; and (iii) oxidative addition to $[\text{Ni}(\text{PMe}_n\text{Ph}_{(3-n)})_2]$. For the case of $[\text{Ni}(\text{PMe}_3)_4]$, a microkinetic model was used to show that these data are consistent with the experimentally-observed ratios of Ni^{I} and Ni^{II} . Importantly, $[\text{Ni}(\text{PMe}_n\text{Ph}_{(3-n)})_2]$ complexes often have little if any role in the oxidative addition reaction because they are relatively high in energy. The behaviour of $[\text{Ni}(\text{PR}_3)_4]$ complexes in catalysis is therefore likely to differ considerably from those based on diphosphine ligands in which two coordinate Ni^0 complexes are the key species undergoing oxidative addition.

Photoactivated reactions

The mechanism of the photoinduced iridium-catalyzed enantioselective trichloromethylation of 2-acylpyridines was computationally studied at the DFT and ONIOM(DFT:MM) levels (Fig. 2). The sign and value of the experimentally reported enantiomeric excess was reproduced (99% vs 95%). The origin of selectivity was identified as the presence of steric repulsion between an attacking trichloromethyl radical and the ligands at iridium in the path leading to the minor enantiomer. Evaluation of hypothetical alternative ligands shows that excessive steric pressure can also hinder the path leading to the major enantiomer, thus reducing overall selectivity.

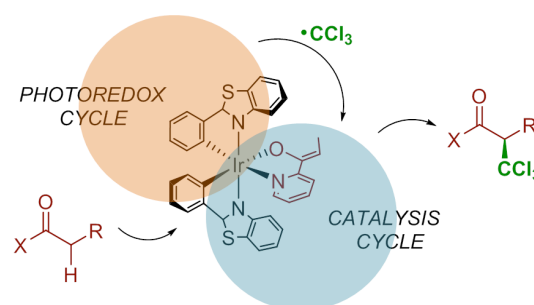


Fig. 2 – Simplified mechanism for the phototinduced enantioselective process

We also analyzed the mechanism of a light-driven enantioselective organocatalytic process

in collaboration with the group of Melchiorre (ICIQ). We reported a photochemical organocatalytic strategy for the direct enantioselective β -benzylation of α,β -unsaturated aldehydes. The chemistry capitalizes upon the light-triggered enolization of 2-alkyl-benzophenones to afford hydroxy-*o*-quinodimethanes. These fleeting intermediates are stereoselectively intercepted by chiral iminium ions, transiently formed upon condensation of a secondary amine catalyst with enals. Density functional theory (DFT) revealed that the reaction proceeds through an unconventional Michael-type addition manifold instead of a classical cycloaddition mechanism, followed by ring-opening.

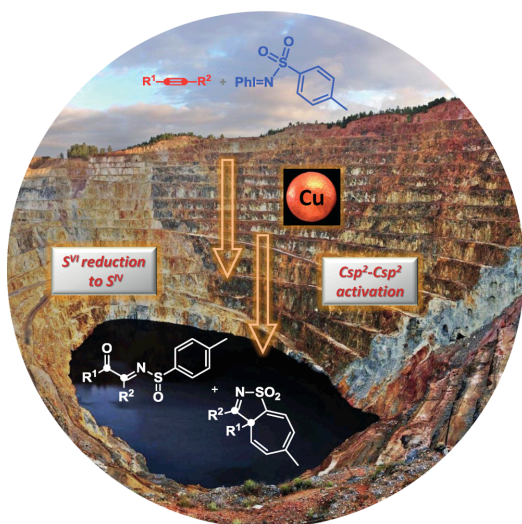
C-C bond formation

A novel reaction involving catalytic nitrene transfer to alkynes was investigated in collaboration with the group of Pérez (Huelva) (Fig. 3). A transformation was reported for the reaction of terminal or internal alkynes with the nitrene precursor $\text{PhI}=\text{NTs}$ (Ts= *p*-toluenesulfonyl) in the presence of catalytic amounts of $\text{Tp}^{\text{Br}_3}\text{Cu}(\text{NCMe})$ (Tp^{Br_3} = hydrotris(3,4,5-tri-bromo-pyrazolyl)borate). Two products containing an imine functionality were isolated from the reaction mixtures, identified as sulfinamides and isothiazoles. The former correspond to the formal reduction of the sulfone group into sulfoxide, whereas the latter involves the insertion of an alkyne carbon atom into the aromatic ring of the N-tosyl moiety.

Fig. 3 – Copper-based complex catalyze the reaction between alkynes and nitrene precursors to yield sulfinamides and isothiazoles.

Calculations reproduced all experimental data with different substrates and produce a picture in which the key difference between internal and terminal alkynes is that formation of a seven-member ring is reversible only for the case of terminal alkynes. The reason for this behavior is very likely related to steric effects.

The intermolecular gold(I)-catalyzed reaction between arylalkynes and alkenes was studied in collaboration with the group of Echavarren (ICIQ). The reaction leads to cyclobutenes by a [2 + 2] cycloaddition, and it takes place stepwise, first by formation of cyclopropyl gold(I) carbenes, followed by a ring expansion. However, 1,3-butadienes are also formed in the case of *ortho*-substituted arylalkynes by a metathesis-type process. The corresponding reaction of alkenes with aryl-1,3-butadiynes, ethynyllogous to arylalkynes, leads exclusively to cyclobutenes. A comprehensive mechanism for the gold(I)-catalyzed reaction of alkynes with alkenes was proposed on the basis of DFT calculations, which showed that the two pathways leading to cyclobutenes or dienes are very close in energy. The key intermediates are cyclopropyl gold(I) carbenes, which were independently generated by retro-Buchner reaction from stereodefined 1a,7b-dihydro-1H cyclopropa[a]naphthalenes.



In an additional collaboration with both the groups of Pérez (Huelva) and Echavarren (ICIQ), we were able to analyze another process involving silver. Silver(I) promotes the highly chemoselective N-amidation of tertiary amines under catalytic conditions to form aminimides by nitrene transfer from $\text{PhI}=\text{NTs}$. Remarkably, this transformation proceeds in a selective manner in the presence of olefins and other functional groups without formation of the commonly observed aziridines or C-H insertion products. The methodology can be applied not only to rather simple tertiary amines but also to complex natural molecules such as brucine or quinine, where the products derived from N-N bond formation were exclusively formed. Theoretical mechanistic studies showed that this selective N-amidation reaction proceeds through triplet silver nitrenes.

Finally, the reaction of carbon dioxide with a-siloxy silanes assisted by cesium fluoride was studied by means of DFT calculations with the B97D functional. Different mechanistic models were examined, including explicit introduction of cationic counterions and solvent molecules. The reaction was confirmed to proceed through carbanionic intermediates generated by Brook rearrangement, a carbon-to-oxygen transfer of a silyl group. The cesium cation was shown to play a critical role in stabilizing the key transition state.

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